REMARKS

The present amendment is in response to the Office Action dated June 16, 2004. Claims 1-10, 14-26, 28, 31-44 and 47-55 are now present in this case. Claims 11-13, 27, 29, 30 and 45 are canceled. Claims 1, 15, 19, 20, 28, 31-33, 38 and 41 are amended. New claims 47-55 are added.

The applicants wish to express their appreciation to the Examiner for the telephone conference with the applicants' attorney on August 26, 2004.

The Office Action has rejected claims 1-40 under 35 U.S.C. § 101 as non-statutory subject matter. These claims have been amended to more clearly recite the invention and are believed clearly to recite technical features that are statutory subject matter. Accordingly, the applicants kindly request that the rejection under 35 U.S.C. § 101 be reversed.

Claims 1-10, 14-18, 20-26, 28, 32, 34-37, 39 and 41-45 stand rejected under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 6,059,724 to Campell et al. The applicants respectfully disagree with the assessment of Campell and its applicability to the claimed invention. Claims 19, 31, 33, 38 and 40 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Campell. Because the aforementioned claims are rejected on the basis of the single reference (*i.e.*, Campell), it is convenient and efficient to discuss the claims generally with respect to Campell.

Discussion of Campell

Campell is directed to a technique for predicting future health of an individual. Campell analyzes biomarkers of an individual subject to determine a future risk that that subject will acquire a selected biological condition within a specified period of time. Campell describes risk as the "a *priori* probability of a specified event within a specified time frame." (See column 3, lines 34-36.) To determine the probability, Campell discloses a technique in which the biomarkers of the individual subject are compared with the biomarkers of a training set. The training set of biomarker data is

acquired using longitudinally acquired biomarker values from individual members of a test population. The individuals within the test population that acquire the specified biological condition within the specified time period (or a general) are classified into one sub-population (*i.e.*, sub-population D) and those individuals being identified as not having acquired the specified biological condition within the specified time period or age interval are classified into a second sub-population (*i.e.*, sub-population D-bar). It should be noted that Campell does not teach or suggest any risk assessment of the test population used to derive the database of reference biomarker values. At the start of the longitudinal time period the test population must be unaffected by the biological condition (see column 18, lines 13-17), but no risk assessment is performed. At the end of the longitudinal study, the population is categorized into the two sub-populations discussed above (*i.e.*, sub-population D and bus-population D-bar). During the development of the database biomarker values, Campell does not teach or suggest any risk analysis to determine whether any of the individual members of the test population were at risk. Thus, at the end of the longitudinal study, Campell retrospectively assigns individual members of the test population to an "affected" sub-population or an "unaffected" sub-population.

At a subsequent point in time, the acquired database of biomarker values are compared with biomarker values of an individual subject to prospectively predict the probability of that individual acquiring the selected biological condition within the specified time frame or age interval. This analysis is done using standard statistical approaches of applying a training model (*i.e.*, the longitudinally acquired biomarker values in the database) with the test data set provided by the individual subject. Thus, Campell is able to prospectively determine the future probability of an individual subject acquiring a selected biological condition. To have any meaningful analysis, the techniques of Campell are applied only to a population of persons who do not have and have not had the specified biological condition. (See column 18, lines 12-14.) For example, it may desirable to determine the probability of death by myocardial infarction. (See column 3, lines 23-26.) Such analysis is a prospective probability analysis

performed by comparing the individual subject's biomarker values with the training set of biomarker values. This is a prospective analysis on unaffected individuals. As noted by Campell, the post-hoc probability of acquiring a selected biological condition is either 0 or 1 (*i.e.*, either the individual did or did not acquire the biological condition). If an individual initially has the selected biological condition, the entire process of Campell becomes irrelevant as there is no need to predict the future probability of acquiring a selected biological condition that has already been acquired. Campell does not teach to suggest any individual or sub-population that can be categorized as "at risk, affected" (ARA). Indeed, Campell has no need for an ARA classification, since such a classification makes the future probability analysis of Campell unnecessary.

It is important to note that Campell does not, at any time, teach or suggest the classification of a population into a sub-population categorized as "at risk," but "unaffected" (ARU). As noted above, the acquisition of training data is performed longitudinally on subjects without any assessment as to whether any individual in the test population is at risk. Thus, the population used for longitudinal study may be considered to have "unknown" risk and "unaffected" status (URU) at the beginning of the study. At the end of the longitudinal study, the subjects are classified into an affected status or unaffected status, but with a still unknown risk. Accordingly, at best these sub-populations may be categorized as "unknown" risk and "unaffected" status (URU) and "unknown" risk, but "affected" status (URA). When applying the training set data to an individual subject, the individual subject initially has an unknown risk status and is unaffected. However, the so-called "risk" analysis performed by Campell is a prospective analysis to determine the probability of that individual acquiring the specified biological condition within the specified time period or age range.

The present invention

The present invention is directed to techniques to identify a target associated with a selected biological condition. The target may, for example, involve diagnostic test related to the biological condition (see page 8, lines 15-20), a vaccine

component (see page 34, lines 14-17), a drug target (see page 8, lines 9-12), or a drug component (see page 8, lines 12-14). The target for a selected biological condition is identified based on an analysis of genetic variation between an at risk, affected (ARA) sub-population compared with an at risk, unaffected (ARU) sub-population. It is important to note that the risk analysis performed by the present invention is a retrospective risk analysis and not a predictive analysis, such as taught by Campell. That is, the present techniques are interested in sub-populations that have been at risk in the past for the selected biological condition. In particular, some portion of the "at risk" population become affected by the biological condition (ARA) while other parts of the at risk population are unaffected (ARU) even though they are at risk and by all known standards, should be affected by the biological condition. It is the hypothesis of the current approach to target identification that genetic differences between the ARA sub-population and the ARU sub-population confer some form of genetic immunity on the ARU population. That is, the ARU sub-population ought to have the selected biological condition but for the genetic variations. Analysis of the genetic differences between the ARA sub-population and the ARU sub-population leads to the identification of targets to be used for diagnostic, vaccine, or therapeutic purposes. Campell does not teach or suggest the segregation of a population into an ARU sub-population. Indeed, Campell has no need for such a sub-population because the goals in Campell are dramatically different than those of the claimed invention.

With respect to individual claims, claim 1 is directed to a computer-implemented method for the identification of diagnostic or therapeutic targets associated with the selected biological condition. The computer is used to analyze stored data related to medical histories of a population and medical test results of the population and recites *inter alia* "based on computer analysis of the data related to the medical histories and the data related to the medical test results, classifying the population into a phenotypic sub-population defined as having a current risk exposure and denoted as at risk and affected (ARA) by the selected biological condition and a phenotypic sub-population defined as having a current risk exposure and denoted as at risk and

unaffected (ARU) by the selected biological condition." The two sub-populations recited in claim 1 both have a current risk exposure for the selected biological condition. The at risk categorization is based on medical histories and medical test results. Campell is directed to a technique for attempting to determine whether a person, at the present time, is likely to have a high probability of acquiring a specified biological condition at some future point in time. In sharp contrast, the present invention, as recited in claim 1, uses the computer analysis of medical histories and medical test results to classify a population that has a current risk exposure rather than the probability of some future risk. That is, the population recited in claim 1 should be affected by the selected biological condition based on medical measures. However, a portion of that population is affected (ARA) while some other portion of the population is unaffected (ARU) even though both sub-populations are at risk and should, by conventional measures, be affected by the selected biological condition. Campell does not teach or suggest such segregation of the populations into ARA and ARU sub-populations.

Claim 1 further recites performing computer analysis of genetic data from the ARA and ARU sub-populations to identify genetic variations therebetween and "using data related to the identified genetic variations between the ARA sub-population and the ARU sub-population to identify the target associated with the selected biological condition." As noted above, Campell does not teach or suggest the segregation of an at risk population into ARA and ARU sub-populations and, therefore, cannot possibly suggest genetic analysis of variations between these two sub-populations to identify a diagnostic or therapeutic target associated with the biological condition. Accordingly, claim 1 is clearly allowable over Campell. Claims 2-10, 14-19, and new claims 47-50 are also allowable in view of the fact that they depend from claim 1, and further in view of the recitation in each of those claims.

Claim 20 is also a method claim directed to a technique for data analysis to identify a target for use in treating a selected biological condition. Claim 20 defines disease characteristics and performs a computer analysis of medical test results and determines the affected status of each of a plurality of subjects based on the analysis.

Claim 20 also recites *inter alia* "defining risk characteristics of the selected biological condition." Claim 20 further recites "based on the risk characteristics, determining a current risk status for each of the plurality of subjects." Based on the affected status and risk scores, the subjects are classified into "a predetermined category for the selected biological condition selected from a group comprising at risk, affected (ARA) and at risk unaffected (ARU)." As discussed above with respect to claim 1, Campell does not teach or suggest any categorization of subjects into ARA and ARU categories. Furthermore, Campell does not teach or suggest any analysis that would define current risk status for subjects. As previously discussed, Campell is only concerned with *a priori* probability of acquiring a biological condition at some point in the future. There is no need or concern by Campell to address current risk status or to categorize subjects at the present time as ARU or ARA. As noted above, an ARA category makes no sense in Campell because there is no need to determine a further probability for an individual that is already affected.

In addition, claim 20 recites performing genetic tests on the subjects and analyzing the test results of the ARU subjects with the genetic test results of the ARA subject to determine genetic differences between the groups and thereby "identifying one or more targets for use in treating the selected biological condition." Campell does not teach or suggest the sub-population groupings of ARA and ARU and, furthermore, does not teach or suggest analyzing genetic test differences between these sub-populations to identify a treatment target, as recited in claim 20. Accordingly, claim 20 is clearly allowable over Campell. Claims 21-26, 28, 31-40 and 51 are also allowable in view of the fact that they depend from claim 20, and further in view of the recitation in each of those claims.

Claim 41 is a system claim for a data analysis system to identify a target for treating a selected biological condition. Claim 41 recites *inter alia* a processor to "accept medical history data from a plurality of subjects and assign current disease risk numeric scores to the medical history data based on the numerical data defining disease risk characteristics of the selected biological condition." Campell does not

suggest any technique for assigning a current disease risk numeric score to medical history data. The processor in claim 41 is further configured to "determine an affected status and a risk status for each of the subjects based on the respective affected status numeric scores and the current disease risk numeric scores." As noted above, Campell only considers future probabilities and does not perform any analysis based on current disease risk numeric scores.

Claim 41 also recites a processor to "based on the affected status and the risk status, classify each of the plurality of subjects into a predetermined category selected from a group of categories comprising at risk, affected (ARA) and at risk unaffected (ARU)." As discussed above, Campell does not teach or suggest categorizations of populations into ARA and ARU categories and makes no determination based on current disease risk numeric scores, as recited in claim 41.

Finally, the processor in claim 41 is configured to "analyze genetic test result data to determine genetic variations between the subjects and the ARA category and the subjects in the ARU category; and identify a target for treating the selected biological condition based on the genetic variations." As previously noted, Campell does not categorize subjects into ARA and ARU categories. Furthermore, Campell does not teach or suggest analyzing genetic test results between the subjects in these categories and does not teach or suggest identifying a target for treating biological condition based on the genetic variations. Accordingly, claim 41 is clearly allowable over Campell. Claims 42-44, 46 and new claims 52-55 are also allowable in view of the fact that they depend from claim 41, and further in view of the recitation within each of those claims.

In view of the above amendments and remarks, reconsideration of the subject application and its allowance are kindly requested. If questions remain regarding the present application, the Examiner is invited to contact the undersigned at (206) 628-7640.

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